

Remarks

Claims 49-52, 55, 60-63, 66, 68, 71-73, 76, 80, 84, 88 and 166-181 are pending in this application and have been rejected by the Examiner. No claims are amended with this response. No new matter is added. Reconsideration and withdraw the outstanding rejections in light of the remarks that follow is respectfully requested.

I. Rejections Withdrawn

Applicants acknowledge and thank the Examiner for withdrawing, in light of Applicants' earlier arguments, the rejection of claims 49-52, 55, 60-63, 66, 68, 71-73, 80, 84 and 166-181 under 35 U.S.C. 112, second paragraph.

II. Claim Rejections Under 35 U.S.C. § 102

Mroczkowski (U.S. 5,137,827)

Claims 49-52, 55, 61-63, 66, 68, 76, 80, 84, 166, 168, and 176-179 were rejected under 35 U.S.C. § 102(b) as being anticipated by Mroczkowski (U.S. Patent No. 5,137,827; hereinafter referred to as "Mroczkowski").

The Examiner based the rejection of claims 49, 55, 63, 66 and 173 on the contention that "the applicant has not recited any structural requirements of the particles other than they contain gold, and have a diameter of 1 to 500 nm inclusive" (Office Action at p. 3, lines 10-12). Applicants respectfully disagree, and assert that the limitation in claim 49 that "the color of scattered light scattered by at least 90% of said particles of each said population upon illumination of each said population on a surface at a particle density of less than 0.1 particles per

μm^2 with white light is indistinguishable to the human eye when viewed with less than 500 times magnification and without electronic amplification,” is a structural limitation. In particular, because the color and intensity of light scattered from Applicants’ light scattering particles is a function of particle size (see, e.g., Application at p. 85, line 24 - p. 87, line 30), the indistinguishability, or relative uniformity, of the color of light scattered from the claimed population of particles dictates that the particle size distribution within each population is relatively homogeneous. Thus, the cited limitation is a structural limitation, and not simply a functional result of arranging a population at a particle density of less than 0.1 particles per μm^2 .

The utility of a particular population of light-scattering particles in the present invention depends upon the population as a whole, and upon the relatively uniform size distribution of particles within the population. This relative homogeneity of size of the light-scattering particles within each population, and the resulting uniformity of the color of scattered light from each population, are useful for identifying and distinguishing, using the naked eye, light scattered by a particular population of scattered light particles. This allows, for example, one to easily distinguish light scattered by a population of particles, e.g., based upon the color of the light scattered by the population, from background scattered light. In multiplexed assays using multiple populations of light-scattering particles having precise dimensional characteristics within each population, one can readily identify and distinguish between one or more analytes in a sample by the color of the scattered light from each population of particles bound to each analyte.

In contrast, Mroczkowski discloses a method for detecting the occurrence of a reaction by measuring a change in an electrical circuit when antibodies with bound electrically-conductive particles react with an antigen. Even though the particles in Mroczkowski may individually scatter light, there is no disclosure in Mroczkowski of any population of light-scattering particles having the particular characteristics as in claim 49 of the present invention. All of the other pending claims depend directly or indirectly from claim 49, and therefore distinguish over Mroczkowski for at least the same reasons as discussed above with respect to claim 49.

With respect to claims 50-52, 61, 62, 68, 76, 80, 84, 166, 168, 176-179, the Examiner states that, although Mroczkowski *et al.* do not specifically recite that antibodies or other additional material does not significantly interact with light in the visible region of the spectrum, “a person of ordinary skill in the art would have known that materials such as protein would not significantly interact with light in the visible region of the spectrum, as is evidenced by applicant’s claims”. In response, Applicants respectfully point out that it is improper for the Examiner to use the applicants own claims as evidence of what is known by one skilled in the art. Applicants also point out that Applicants themselves performed tests to determine that different types of macromolecular substances such as antibodies, nucleic acid receptors, or similar substances can be coated on the surface of the particles without significantly altering the scattered light properties of the particles, (see, e.g., p 46, lines 1-30 and p. 291, lines 1-30). Thus, since Applicants deemed it necessary to perform the tests disclosed in the application, the Examiner can not properly impute knowledge of the results of such test onto one of ordinary skill in the art.

For at least the reasons discussed above, Applicants respectfully request that the rejection of claims 49-52, 55, 61-63, 66, 68, 76, 80, 84, 166, 168, and 176-179 under 35 U.S.C. § 102(b) as anticipated by Mroczkowski be reconsidered and withdrawn.

Rembaum (U.S. 4,929,400)

Claims 49-52, 55, 60, 63, 66, 71-73, 76, 80, 84, 88, 166, 168-173, and 176-179 were rejected under 35 U.S.C. § 102(b) as being anticipated by Rembaum (U.S. Patent No. 4,929,400; hereinafter referred to as “Rembaum”). Like Mroczkowski, Rembaum fails to disclose or suggest populations of particles having any of the particular light-scattering characteristics as claimed by the Applicants. In particular, as discussed above, the claimed populations have specific light-scattering characteristics (e.g., color and intensity) that are a function of the narrow distribution of particle sizes within each population. Such structural characteristics are embodied by the limitation that “the color of scattered light scattered by at least 90% of said particles of each said population upon illumination of each said population on a surface at a particle density of less than 0.1 particles per μm^2 with white light is indistinguishable to the human eye when viewed with less than 500 times magnification and without electronic amplification...”.

In contrast, Rembaum teaches a method of making polymeric microspheres by creating a spheroid droplet of liquid and exposing the droplet to polymerizing radiation. The droplets may contain a dispersion of small filler particles, such as magnetic metal particles of various types. Thus, as with Mroczkowski, Rembaum provides no disclosure, teaching or even suggestion of populations of light scattering particles having any of the distinct light-scattering characteristics of the populations of particles of Applicants independent claim 49.

Claims 50-52, 55, 60, 63, 66, 71-73, 76, 80, 84, 88, 166, 168-173, and 176-179 depend directly or indirectly from claim 49, and distinguish over Rembaum for at least the same reasons as claim 49. Accordingly, Applicants respectfully request that this rejection under 35 U.S.C. § 102(b) be reconsidered and withdrawn.

Margel (U.S. 4,624,923)

Claims 49-52, 55, 61-63, 66, 68, 71-73, 76, 80, 84, 166-173 and 176-179 were rejected under 35 U.S.C. § 102(b) as being anticipated by Margel et al. (U.S. Patent No. 4,624,923; hereinafter referred to as “Margel”). Margel describes metal-containing polyaldehyde microspheres that may be radioactive or magnetic. However, like Mroczkowski and Rembaum, Margel fails to disclose or suggest one or more populations of particles having any of the particular light-scattering characteristics as recited in Applicants’ independent claim 49.

Claims 50-52, 55, 61-63, 66, 68, 71-73, 76, 80, 84, 166-173 and 176-179 depend directly or indirectly from claim 49, and distinguish over Rembaum for at least the same reasons as claim 49. Accordingly, Applicants respectfully request that this rejection under 35 U.S.C. § 102(b) be reconsidered and withdrawn.

Tarcha (U.S. 5,567,628)

Claims 49-52, 55, 62, 63, 66, 68, 76, 80, 84, 166-173, and 176-181 were rejected under 35 U.S.C. § 102(e) as being anticipated by Tarcha et al. (U.S. Patent No. 5,567,628; hereinafter referred to as “Tarcha”). As mentioned by the Examiner, Tarcha teaches gold colloids. However, as with Mroczkowski, Rembaum, and Margel fails to disclose or suggest

one or more populations of light-scattering particles of particular narrow size distributions, such that “the color of scattered light scattered by at least 90% of said particles of each said population upon illumination of each said population on a surface at a particle density of less than 0.1 particles per μm^2 with white light is indistinguishable to the human eye when viewed with less than 500 times magnification and without electronic amplification...”, as in Applicants’ independent claim 49.

Moreover, Tarcha teaches that, although different methods of preparation of metal colloids can affect the appearance and intensity of the resulting Raman spectra (e.g., due to differences in the dimensions of the colloids), this is not a limiting factor with respect to the invention. Thus, Tarcha does not teach or suggest one or more populations of light-scattering particles having dimension within narrow tolerance ranges required to provide scattered light of precise colors as claimed in the present invention.

Claims 50-52, 55, 62, 63, 66, 68, 76, 80, 84, 166-173, and 176-181 depend directly or indirectly from claim 49, and distinguish over Tarcha for at least the same reasons as claim 49. Accordingly, Applicants respectfully request that this rejection under 35 U.S.C. § 102(e) be reconsidered and withdrawn.

III. Claim Rejections Under 35 U.S.C. § 103 (a)

Mroczkowski (U.S. 5,137,827)

Claims 60, 88, 174 and 175 were rejected as being unpatentable over Mroczkowski (U.S. 5,137,827). In making this rejection, the Examiner acknowledges that Mroczkowski fails to disclose a population of particles characterized by a coefficient of variation of less

than 5%. However, the Examiner goes on to state that it would have been obvious to one of ordinary skill in the art to have a coefficient of variation of less than 5% for the microspheres of Mroczkowski, as “discovering the optimum or workable ranges involves only routine skill in the art”. Essentially the same rationale is used by the Examiner to assert that it would have been obvious to have coatings of particular dimensions as in claims 174 and 175.

Applicants respectfully disagree, and point out that the electrically-conducting particles of Mroczkowski have a completely different purpose than the populations of light scattering particles of the present claims, as described above. Thus, there is nothing in Mroczkowski or anywhere else to teach or suggest modifying the microspheres of Mroczkowski to form one or more populations of particles having particular “optimum or workable ranges”, let alone for the purpose of optimizing light-scattering characteristics of each population.

Establishing *prima facie* obviousness requires a showing that each claim element is taught or suggested by the prior art. *See In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Specifically, establishing *prima facie* obviousness requires a showing that some combination of objective teachings in the art and/or knowledge available to one of skill in the art would have lead that individual to arrive at the claimed invention. *See In re Fine*, 5 USPQ2d 1596,1598 (Fed. Cir. 1988). Moreover, establishing *prima facie* obviousness requires not only a showing that such a combination of prior art teachings is possible, but also that the teachings would have 1) motivated the skilled artisan to make the combination to arrive at the claimed invention, and 2) suggested to the skilled artisan a reasonable likelihood of success in making and using the claimed invention. *See In re Dow Chem. Co.*, 837 F.2d

469, 473 (Fed. Cir. 1988). Absent a showing of such motivation and suggestion, *prima facie* obviousness is not established. *See Fine*, 5 USPQ2d at 1598.

Since Mroczkowski neither discloses nor suggests the particular light scattering characteristics of the claimed populations of particles, a *prima facie* case of obviousness has not been established for any of claims 60, 88, 174 or 175. Applicants therefore respectfully request that the rejection of claims 60, 88, 174 and 175 under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

Margel (U.S. 4,624,923)

Claims 60, 88, 174 and 175 were rejected as being unpatentable over Margel (U.S. 4,624,923). As with Mroczkowski, Margel neither discloses nor suggests the particular light scattering characteristics of the claimed populations of particles, and therefore a *prima facie* case of obviousness has not been established for any of claims 60, 88, 174 or 175. Applicants therefore respectfully request that this rejection under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

Margel (U.S. 4,624,934) in view of Tarcha (U.S. 5,567,628)

Claim 181 was rejected as being unpatentable over Margel (U.S. 4,624,934) in view of Tarcha (U.S. 5,567,628). Claim 181 depends indirectly from independent claim 49, and includes additional limitations with respect to antibodies within the population of particles. As discussed above, Margel neither discloses nor suggests the particular light scattering characteristics of the claimed populations of particles, and therefore a *prima facie* case of

obviousness has not been established for claim 181. Applicants therefore respectfully request that this rejection under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

Tarcha (U.S. 5,567,628)

Claims 60 and 88 were rejected as being unpatentable over Tarcha (U.S. 5,567,628). As with Mroczkowski and Margel, and as discussed above with respect to the 35 U.S.C. § 102(e) rejections, Tarcha neither discloses nor suggests the light scattering characteristics of the one or more populations of particles of claim 49, which recites that “the color of scattered light scattered by at least 90% of said particles of each said population upon illumination of each said population on a surface at a particle density of less than 0.1 particles per μm^2 with white light is indistinguishable to the human eye when viewed with less than 500 times magnification and without electronic amplification...” Therefore, a *prima facie* case of obviousness has not been established for either of claims 60 or 88. Applicants therefore respectfully request that this rejection under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

Conclusion

For all of the foregoing reasons, reversal of the rejections of claims 49-52, 55, 60-63, 66, 68, 71-73, 76, 80, 84, 88 and 166-181 is respectfully requested. Applicants respectfully request that the above-mentioned amendments and remarks be entered and made of record in the file history of the subject application.

It is not believed that any fees are required beyond those that may otherwise be provided for in documents accompanying this paper. However, should the Patent Office determine otherwise, please charge the required fee to Jones Day deposit account no. 50-3013, referencing Docket No. 11032-021-999 (CAM No. 107168-999020).

Respectfully submitted,

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Laura A. Coruzzi 30,742
Laura A. Coruzzi (Reg. No.)

By: Richard E. Ballard 46,078
Richard E. Ballard (Reg. No.)

JONES DAY
222 East 41st Street
New York, New York 10017-6702
(212) 326-3939